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13. ABSTRACT (Maximum 200 words)

Depression, anxiety and heart failure: A review

Short title: Depression and anxiety in heart failure

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Abstract

Background: Although common among patients with heart failure, depression and anxiety have

been relatively neglected by researchers and practitioners. Both depression and anxiety have been

implicated in contributing independently to the poor outcomes seen in patients with heart failure.

Emphasis in the literature is on physical symptom recognition and management, in contrast to the

patient's perspective of the effects of heart failure on his/her daily life.

Methods: This review summarizes and integrates research findings on anxiety and depression

and translates these findings to clinical practice.

Results: Depression and anxiety are prevalent among patients with heart failure, and require

assessment and intervention. Short-term nonpharmacologic approaches, in conjunction with drug

therapy, hold promise in for successful management of patients who are depressed and or

anxious.

Conclusions: Carefully designed clinical trials that are tailored to individual needs, yet are

embedded within a systemic framework, are needed to inform clinicians regarding optimal

practices for the treatment of patients with heart failure who suffer from depression and/or

anxiety.

Key words: heart failure, depression, anxiety, cognitive behavioral therapy

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"It is necessary not only to say something about what conditions people are experiencing but also to understand the impact these conditions have on their life."

Approximately 250,000 individuals die as a consequence of heart failure (HF) each year, and the number of HF deaths has increased six fold during the past 40 years.² It is the leading cause for hospitalization in individuals 65 years and older, and the most costly cardiovascular disease in the U.S., with estimated costs exceeding 20 billion.²⁻⁴ Although HF has been described as "a new epidemic" with more than five million Americans identified and 500,000 newly diagnosed with HF annually, it has also been identified as a "last frontier" of behavioral cardiology.

Psychosocial issues, particularly depression and anxiety, in patients with HF have been relatively neglected by researchers and practitioners. Emphasis in the literature is on symptom recognition and management, in contrast to the patient's perspective of the effects of heart failure on his/her daily life. The focus of this review was to summarize and integrate research findings on anxiety and depression, mood states that have been implicated in HF course and outcome, and to translate these findings to clinical practice. This review will also focus on a of lived experiences of patients struggling with the emotional and life-altering effects of previous weakness in the literature, failure to address anxiety and depression associated with HF from the perspective HF. Representation of the perspective HF. Representation of

Depression and Heart Failure

Clinical depression is a disorder of mood, consisting of a combination of elements that interfere with a person's ability to perform his/her day-to-day functioning. A diagnosis of major depression requires the presence of five or more of the following symptoms for a two-week period: (1) depressed mood; (2) markedly diminished interest or pleasure in all or nearly all activities; (3) significant weight loss or gain, or a decrease or increase in appetite; (4) insomnia or hypersomnia; (5) fatigue or loss of energy; (6) feelings of worthlessness or excessive or inappropriate guilt; (7) diminished ability to think or concentrate or indecisiveness; and /or (8)

recurrent thoughts of death, suicidal ideation, or suicide attempt. One of the symptoms must include depressed mood and/or loss of interest or pleasure, and the symptoms must reflect a change in functioning resulting in social, occupational, or other life impairment.⁹

Depression is the most prevalent psychiatric condition, a finding that is consistent across the world. Relapse and recurrence following successful treatment of depression are common.

Segal and associates conclude that the risk for repeated episodes exceeds 80%, with patients experiencing an average of four major depressive episodes, each of 20 weeks in duration.¹⁰

Up to 5 billion of the total 20 billion costs associated with HF during 1998 may be associated with depression. Sullivan et al analyzed health care costs for three groups totaling 10,980 patients (no depression, antidepressant prescription only, and antidepressant prescription and depression diagnosis recorded), in a 3-year retrospective study of a health maintenance organization. Covariates were age, sex, medical comorbidity, and length of hospitalization stay. Hospitalization costs were 26% higher in the antidepressant prescription only group, and 29% higher in the antidepressant prescription and depression diagnosis recorded group, in comparison to the no depression group. Increased costs were attributed to increased inpatient and outpatient utilization and *not* increased mental health utilization. The authors concluded that depression and other conditions requiring the use of antidepressant medications contribute significantly to the direct medical costs for HF care.

Depression is associated with increased mortality. Vaccarino et al, and Murberg et al reported that level of depression is linearly related to 6-month and 2-year mortality rates, respectively. 11, 12 Moderately and severely depressed patients with HF are reported to have significantly higher mortality than mildly and nondepressed patients with HF. Patients with severe depression are four times more likely to die within two years compared to those classified as not depressed.

There is growing evidence that the prevalence of depression is high and may be increasing in individuals with HF. The prevalence of depression among patients with HF ranges

from 15% to 36%, although rates as high as 77.5% have been reported. The rate of depression in individuals varies according to population studied, method of diagnosis, and the classification of depression. In addition, reported rates of depression vary based on the contexts in which they are assessed (i.e. hospital versus home). Nevertheless, rates are significant, and if undetected and untreated, account for substantial additional treatment costs associated with HF.

Thomas et al.⁴ summarized the findings of eight recent studies of depression among patients with HF. Analysis of methodology revealed that different methods of assessing depression resulted in different prevalence rates. The lowest rates of depression among hospitalized patients were reported using the Depression Interview Schedule, an instrument designed to identify major depression. These rates were reported by Freedland and associates, and Jiang and associates as 20% and 13.9%.^{21, 22} Using the Beck Depression Inventory (BDI), more than twice as many individuals with HF were identified as depressed.²²

Hospitalization status affects reports of depression. A relatively consistent finding is that hospitalized patients with HF report higher rates of depression than stabilized outpatients. Among hospitalized patients with HF, depression rates ranged from 13.9%²² to 77.5%. Among outpatients with HF, depression rates ranged from 13%²³ to 48%.

Given that patients with HF frequently cycle between periods of stabilization and periods of hospitalization, depressive symptoms may also change in the short term, depending on the patient's health and functional status during hospitalization and 4 to 6 weeks post discharge.⁴

Depression is also related to severity of HF symptoms. Baseline functional status, including limitation in activities of daily living and dyspnea at rest, are strongly related to depression.¹²

Friedman and Griffin reported significant correlations between depression severity and increased physical symptoms or decreased physical functioning.¹⁷

Interpretation of results relating depression and HF are subject to selection bias, likely resulting in underestimates of the reported relationship between depression and HF.¹⁶ Not all invited patients choose to participate, and those who do participate tend to be healthier and less

prone to complain about functional limitations, in comparison those who do not choose to participate. It is also likely that those who do participate are less inclined to be depressed than those who decline to participate. In addition, studies do not typically include somatic depression symptoms of fatigue and insomnia. While they are symptoms of depressive state, they are also primary symptoms of HF and most studies do not analyze data both with and without these criteria, although there are exceptions.²⁵

Anxiety and Heart Failure

Anxiety is a negative affective state resulting from an individual's perception of threat and characterized by a perceived inability to predict, control or gain the preferred results in given situations. ²⁶ Anxiety is a distinct emotional experience that has cognitive, neurobiological and behavioral components, and that arises out of the interaction of an individual with the environment.

²⁷ It, like other emotions, allows flexibility in behavioral responses to a changing environment.

Anxiety is considered an adaptive process until its magnitude or persistence render it a dysfunctional response that can have negative consequences.

Anxiety exists on a continuum from normal to pathological, and there are a number of anxiety disorders (i.e. panic disorder, phobic anxiety, generalized anxiety, anxiety reactions, chronic anxiety). Nonetheless, research to date strongly suggests that anxiety along the continuum from normal anxiety reactions to pathological have comparable cognitive, neurobiological, and behavioral components, and that clinical anxiety and sub-clinical anxiety are not fundamentally different phenomena. Phenomena. 26-29

Although there is considerably less research on anxiety than on depression in HF, existing evidence suggests that the prevalence of anxiety may be as high as 63% depending on the subgroup of HF patients studied.³⁰ As many as 40% of HF patients may suffer from major anxiety and overall anxiety levels are 60% higher than levels seen in healthy elders.^{31, 32} Compared to

other cardiac patients and patients with cancer or lung disease, patients with HF have similarly high or worse anxiety levels.^{30, 33} Although anxiety may be an expected and even normal reaction to the diagnosis of a serious chronic illness like HF, anxiety in patients with cardiac disease is not benign if it persists or is extreme.^{27, 34-42}.

Only a few investigators have evaluated the association of anxiety with HF patient outcomes ^{16, 43, 44} and the results of these investigations have been mixed. Anxiety predicted functional status at 1 year in patients with HF⁴⁴, but not rehospitalization or mortality. ⁴⁵ However, in a study of patients with recent acute myocardial infarction (AMI) and depressed left ventricular function, anxiety was associated with a higher incidence of adverse cardiac events and cardiac death in the subsequent 6-10 years. ⁴⁶ This inconsistency mirrors that seen in the study of the association between anxiety in patients with CHD and the risk of subsequent CHD events.

Among these studies, four demonstrated that increased anxiety predicted subsequent CHD events (i.e. reinfarction, unstable angina, CHD mortality) ^{32, 47-49}, three reported no association between anxiety and CHD outcomes ^{38, 50-52}, and in one study anxiety was associated with a survival *advantage*. ⁵³ Reasons for these inconsistencies may include the use of multiple different definitions and measures of anxiety.

Proposed Mechanisms Linking Depression and Anxiety with Poor Outcomes.

Reasons for the association between depression and anxiety, and adverse outcomes in patients with HF are not well understood. While some advocate that negative emotions may be a risk factor for HF, others suggest that HF may activate anxiety or depression or that perhaps there exists an interactional effect whereby negative emotions and HF impact one another in deleterious ways. To date there are few studies examining the mechanisms whereby depression or anxiety might be associated with morbidity and mortality outcomes in patients with heart failure, but the evidence in patients with heart disease likely is relevant to HF. There are two pathways proposed linking depression or anxiety and adverse outcomes in patients with heart disease: 1) behavioral; and 2) physiologic (see Figure 1). 27, 29, 34, 35, 41, 47, 54-57

Physiologic mechanisms: Sympathetic nervous system activation. Excess activation of the sympathetic nervous system (SNS) is strongly associated with increased morbidity and mortality in HF. Recent studies of the biology of negative emotions suggest that alterations in autonomic nervous system modulation, particularly the SNS, may partially explain the link with poor outcomes. Anxiety and depression, and the mental stress associated with them are associated with excessive activation of the SNS, and catecholamine release, evidenced by decreased heart rate variability and increased plasma norepinephrine in both healthy persons and individuals with poor health. In addition, baroreflex control is impaired in anxious cardiac patients compared to those with no anxiety.

Sympathetic nervous system activation may result in poor cardiac outcomes through a number of pathways. It is associated with platelet aggregation, volume contraction, increased coagulation and recurrent thrombus formation. A7, 70-75 Thus, SNS activation contributes to thrombogenesis. Electric instability is another consequence of SNS activation and thus enhanced sympathetic stimulation is one cause of cardiac dysrhythmias for patients with cardiac disease. Actually actually

Behavioral effect of depression: Nonadherence. Another possible explanation for the link between depression or anxiety and increased risk of death or rehospitalization is the effect of these emotions, particularly depression, on patient adherence. Nonadherence to HF treatment

plans is common. 98-103 Poor adherence increases the risk of mortality and morbidity in patients with CHD and HF. 104-107 In 42% to 64% of HF readmissions, lack of adherence to prescribed medication and/or diet plans has been implicated as the proximate cause of the readmission. 98, 99, 102, 108

Accumulating evidence indicates that depression may explain partially this high rate of nonadherence. Depression is associated with poor adherence to drug, diet and exercise recommendations in patients with CHD.^{109, 110} Chronically ill patients with depression are three times as likely to be nonadherent to their treatment regimes as those without depression.¹¹¹ Among patients with HF, mental health was a significant predictor of dietary and exercise adherence.¹⁰⁴

Pharmacological Interventions for Depression and Anxiety

Identification and management of depression and anxiety is "crucial" to the treatment of HF. 112 Jacob and Sebastian studied the pattern of antidepressants, anxiolytics, and other sedative-hypnotics prescribed during the course of non psychiatric hospital stays in patients with HF. 112 Only 7.9% were prescribed antidepressants, 20.5% received benzodiazepines and 8.2% received Benadryl. The authors concluded that antidepressants are not being prescribed adequately based on the rate of depression in this population of patients. They suggested the possibility that increased use of benzodiazepines and Benadryl is due to HF patients being treated for probable anxiety, irritability, and/or lack of sleep. The overlapping symptoms of fatigue, apathy, and anergia make it more difficult to adequately diagnose depression in patients with HF. The authors conclude that the underutilization of antidepressants may be due to under-recognition of symptomatology and/or under-treatment of depression. They recommend incorporation of questions to rule out depressive symptoms in routine evaluation protocols. Multi-center studies are needed to investigate how, and under what conditions, pharmacological treatments (i.e. SSRIs) can improve outcomes in patients with HF.

Cognitive-behavioral therapy and SSRIs have been demonstrated to be efficacious in primary care patients with mild depression. ¹¹³ There are no controlled studies for patients with HF, with mild or severe depression. Since depression and anxiety may affect autonomic tone and produce decrease heart rate variability, some argue that SSRI use is "justified" given that SSRIs normalize heart rate variability. ¹¹² Newer SSRIs have been shown to have minimal or no cardiac side effects, but the risk in patients with HF has not been systematically tested. ¹¹⁴⁻¹¹⁷ It may be that a combination of treatment with SSRIs and therapy may demonstrate the best outcomes, but this prospect needs to be tested in controlled clinical trials. ¹¹²

Nonpharmacologic Interventions

Heart failure often is a profound source of psychological distress for both patients and their support systems. Women coping with HF report bearing a greater proportion of burden than men, both in the role of patient and spouse. Given the prevalence and impact of depression and anxiety on patients diagnosed with HF, this section will address these emotional states associated with HF from the perspective of lived experiences of patients struggling with the emotional and life-altering effects of HF.

The nonpharmacologic intervention literature with respect to HF is sparse. There is need for evidence-based practices that have proven effective in addressing the life-altering effects of HF. Currently, interventions tend to draw from existing practices related to patients with associated cardiac difficulties such as acute myocardial infarction. In addition, interventions tend to implement "one-size fits all" practices, at the expense of sufficiently tailored interventions to meet the individual and unique needs of the patient. What is needed are diverse models of intervention that have embedded within them individually-tailored interventions that also utilize a systemic framework. In addition, coping style, issues related to meaning systems of the patient, social support, and religious and spiritual orientation of the patient are critical in designing interventions for patients with HF.

Coping Style. Coping style has been implicated as a predictor of disease course and outcome in HF patients. Murberg and Bru found that behavioral disengagement predicted mortality risk in 119 clinically stable patients with symptomatic heart failure within a two-year follow-up period, after controlling for severity of HF, functional status (NYHA), sex, and age. These results mirror those reported by Konstam et al. Disengagement occurs in the context of a disease course which includes physical incapacity, possible loss of roles, and fear and uncertainty about the future. Exploration of counseling tools that would increase the likelihood of HF patients becoming more actively engaged is critically needed. Specifically, development of counseling tools that increase the individual's motivation to effectively manage their heart failure are needed, particularly given the importance of the patient taking action (i.e. adherence to dietary and exercise regimens), and given the fatal nature of the disease.

Meaning. The idea that a sense of meaning and purpose is important to emotional well-being has been documented. Reker examined the unique, combined and interactive contribution of existential variables (personal meaning, choice/responsibleness, optimism) with respect to predicting depression in elderly individuals residing in community and institutional settings. He found that personal meaning, optimism, social resources, and physical health predicted depression in institutionalized elderly. He concluded that existential paradigms in addition to stress paradigms can "... broaden our understanding and appreciation of the experience of depression in older adults" (p. 714). Meaning-centered counseling provides a framework to assist individuals encountering "crisis in meaning". Further exploration of the need for a shift in paradigm, a shift that addresses both meaning systems and coping strategies is key. Helping patients develop and refine meaning systems that enable and empower them to deal more effectively with the disease process appear to be an important avenue for further inquiry for patients with HF. 123

<u>Self-efficacy and perceived control</u>. Research findings indicate that patients who believe in their ability to alter health-related behavior are more likely to engage in behaviors that are

associated with medical well being. 124 Tsay and Chao assert that individuals with high levels of perceived self-efficacy better manage their HF, which in turn leads to improvement in functional status, which in turn leads to improved emotional functioning (i.e. decrease in depression). 13 Their results support the direct and indirect effects of perceived self-efficacy on depression, accounting for 46% of the variance. It is important to note that several limitations were evident in the Tsay and Chao study, including utilization of a Taiwanese population sample that not only was diagnosed with HF, but at least one additional chronic illness, thus limiting generalizability. 13 However, their findings mirror those reported by other investigators supporting the relationship between self-efficacy and functional status. 125, 126

Perceived control includes the perception that one can effectively respond to unpleasant situations either behaviorally or cognitively with the goal of minimizing the aversiveness associated with the situation. 127-129 It is thought that perceived control reduces helplessness, thus counteracting feelings of vulnerability and uncertainty, and reducing feelings of anxiety and depression. 130 Perceived control among cardiac patients, including those with heart failure, is associated with fewer depressive and anxiety symptoms, ^{39, 123} higher self-esteem, and overall greater satisfaction with life. 129, 131 Perceived control increases the likelihood that one will actively engage with the environment to improve the outcome of a distressing situation or event. It can be argued that perceived increase in control can lead to increased engagement with the environment, including increase in active coping skills and better compliance with drug, dietary, and exercise regimens. 132 Bohachick and associates state that "...interventions that foster personal control may well hold the key to reducing poor psychological and functional outcomes" (p. 49). 129 Self-efficacy training for patients with HF to improve patients' confidence in their ability to engage in activities leading to improved functional status appears to be a fruitful endeavor. For example, currently there is lack of data suggesting when and how to assist patients with issues related to functional status. Questions remain relating to timing of nonpharmacologic and pharmacological interventions (i.e. at what juncture should pharmacological interventions be

entertained, in addition to cognitive behavioral interventions that address distorted thought patterns regarding functional status). Data-driven guidelines are needed to inform practitioners how to optimally proceed with HF patients who are clinically anxious and/or depressed.

Social support. An important resource in coping with HF is social support. ^{118, 133} Social support provides a vehicle by which patients can experience a sense of well-being. In addition, social support can assist the individual in counteracting avoidance coping behaviors such as denial and behavioral disengagement, behaviors that are associated with poorer health outcomes for patients with HF. ¹³⁴

Bohachick et al suggest that successful nonpharmacologic interventions need to focus not only on reinforcing personal control, but also on building and maintaining networks of helpfulness and attachments. Patients should be encouraged to renew social relationships that have been neglected as well as build on new social relationships. Support groups can provide a vehicle for the expression and validation of concerns, one possible modality that can influence reduction of feelings of anxiety and depression.

Family Dynamics. The quality of significant relationships in the patient's life is a relevant lens from which to understand how patients and their spouses cope with HF.⁶ In a study involving 128 male and 49 female HF patients and their spouses, Rohrbaugh et al. found that 57% of patients and 40% of their spouses reported being distressed, as assessed by the Hopkins Symptom Check List-25.⁶ The patient's distress was related to severity of illness. Results highlighted the contextual nature of HF distress, suggesting that role differences in distress vary by gender. Potentially important mediating variables such as level of spousal activity restriction¹³⁵ and the partners' styles of relationship-focused coping¹³⁶, and changes in their role responsibility dynamics, and adequacy of the couple's contact with the medical system¹³⁷were not assessed. Results were biased toward couples who could endure an intensive regimen of home interviews. Family support, traditionally measured as spousal support, appears to be critical when considering HRQL in patients with HF.¹³⁸ Further studies are needed to expand our knowledge of family

dynamics to empower family members and significant others to decrease distress associated with HF.

Religiosity/spirituality/ Religiosity/spirituality has been acknowledged recently in the literature as an additional factor that may influence adaptation to illness. ¹³⁹⁻¹⁴¹ Despite the fact that religiosity/spirituality is an integral component in the lives of most Americans (90% of Americans classify themselves as being "religious"), it is a neglected resource. ¹³⁹ Only 1% of all articles on coping with stressful life events included a religious/spiritual component. ¹³⁹

Although results are inconsistent, studies suggest that individuals who report higher levels of religiosity/spirituality respond to illness with better coping and/or improved adjustment and HRQL, in comparison to individuals who report lower levels of religiosity/spirituality. Research specifically related to coronary artery bypass surgery suggests that religiosity/spirituality not only is implicated in patients' well being, but is also implicated in post-operative length of stay. Research that moves the field beyond global religiosity/spirituality indicators to a more complex, thorough assessment of religiosity/spirituality and HRQL in patients with HF is needed.

To summarize, with respect to behavioral interventions, research conducted over the past twenty years supports the use of cognitive-behavioral approaches in the treatment of depression and anxiety. Patterns of cognitive behavior therapy (CBT) that have been identified as key to positive outcome in depression, but appear to be applicable to anxiety as well, include: (1) providing rationale for treatment; (2) providing highly structured and clear plans for change, including the provision of a sense of control; (3) providing feedback and support so that individuals can receive support and attribute improvement to their own abilities and efforts; and (4) teaching skills that increase personal effectiveness and independence.

CBT provides HF patients with opportunities to monitor thoughts related to their disease, some of which may be non-adaptive, and formulate alternative ways of viewing and acting with respect to managing their disease. For example, patients may hold limiting ideas regarding their

functional capacities which can be challenged. Behaviors that reflect more accurate assessment of functional capacities can be supported by the clinician.

Guck et al. provide treatment suggestions for depressed patients with HF. ¹⁴⁴ They suggest CBT be implemented when depression is: (l) not severe or chronic; (2) psychotic features are absent; (3) previous response to CBT has been positive; (4) medical contraindications to medications exists; and (5) recovery has not been achieved with medication alone. ¹⁴⁴ Antidepressants may be considered when depression is severe, chronic or recurrent, psychotic features are present, previous positive response to medication, family history of depression, and/or patient is unable to do the work required in psychotherapy. A combination of CBT and medication may be indicated when symptoms of depression are severe or chronic and do not respond to therapy or if other psychosocial problems are present. ¹⁴⁴ It is important to note that the above guidelines are suggestions and are not based on well designed studies with clinically depressed HF patients. To date, guidelines based on clinical trials for anxious and/or depressed patients with HF have not been developed.

Conclusions and recommendations

Depression and anxiety are prevalent among HF patients, and in order to enhance adaptation and decrease patients' risk of subsequent HF exacerbations or other cardiac events, depression and anxiety clearly need to be routinely assessed. One of the most important areas for future research is elucidating the mechanisms, physiological and/or behavioral, by which anxiety and depression cause poorer outcomes. Research in this area is important to help clinicians determine the best ways to manage HF patients. For example, without understanding the basic underlying mechanisms related to anxiety, it is difficult to know whether treatment should concentrate on pharmacological strategies such as beta-blocker therapy to decrease sympathetic nervous system responses to anxiety, or focus more directly on anti-anxiety drug therapy.

There is a need to acknowledge relapse rates in the literature on depression and anxiety in HF, particularly given the episodic nature of depression and anxiety. The treatment focus is on a

quick fix without adequate acknowledgement of the chronic and/or episodic nature of both depression and anxiety and how they interface with HF. Although we are becoming increasingly sensitive to the role of depression and anxiety in patients with HF, there continues to be a need to focus research and clinical efforts in a direction that incorporates and is consistent with the complexities and realities of lived experiences of patients with HF.

Short-term approaches such as anxiety management training and CBT interventions developed specifically for depression and anxiety can assist patients to identify cognitive and bodily cues of the onset of anxiety and depression. HF patients can be taught to develop responses that can result in the reduction or elimination of symptoms. Teaching relaxation and cognitive coping skills such as cognitive restructuring of negative cognitions can be helpful and empowering to patients adapting to HF. Approaches need to be individually tailored to address the motivation levels of HF patients who are depressed and/or anxious. Carefully designed clinical trials, that are tailored to individual needs, yet are embedded within a systemic framework, are needed to inform clinicians regarding optimal practices for the treatment of HF patients who suffer from depression and/or anxiety.

References

- 1. Dolan P. Valuing health-related quality of life. Issues and controversies. *Pharmacoeconomics*. 1999;15:119-127.
- 2. American Heart Association. *Heart disease and stroke statistics--2005 update*. Dallas, TX: American Heart Association; 2005.
- 3. Sullivan M, Simon G, Spertus J, Russo J. Depression-related costs in heart failure care. *Arch Intern Med.* 2002;162:1860-1866.
- 4. Thomas SA, Friedmann E, Khatta M, Cook LK, Lann AL. Depression in patients with heart failure: physiologic effects, incidence, and relation to mortality. *AACN Clin Issues*. 2003;14:3-12.
- 5. Moser DK. Psychosocial factors and their association with clinical outcomes in patients with heart failure: Why clinicians do not seem to care. *Eur J Cardiovasc Nurs.* 2002;1:183-188.
- 6. Rohrbaugh MJ, Cranford JA, Shoham V, Nicklas JM, Sonnega JS, Coyne JC. Couples coping with congestive heart failure: role and gender differences in psychological distress. *J Fam Psychol.* 2002;16:3-13.
- 7. Zambroski CH, Moser DK, Roser L, Heo S. Symptoms and symptom management of patients with heart failure who receive hospice care at the end of life (abstract). *Circulation*. 2003;108:IV-503.
- **8.** Zambroski CH, Moser DK, Roser L, Heo S, Chung M. Patients with heart failure who die in hospice. *Am Heart J.* in press.
- 9. Seligman L. Selecting effective treatments: A comprehensive systematic guide to treating mental disorders. San Francisco: Jossey-Bass; 1998.
- 10. Segal SZ, Williams JMG, Teasdale JD. Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse. New York: Guilford Press; 2002.
- 11. Murberg TA, Bru E, Svebak S, Tveteras R, Aarsland T. Depressed mood and subjective health symptoms as predictors of mortality in patients with congestive heart failure: a two-years follow-up study. *Int J Psychiatry Med.* 1999;29:311-326.
- 12. Vaccarino V, Kasl SV, Abramson J, Krumholz HM. Depressive symptoms and risk of functional decline and death in patients with heart failure. *J Am Coll Cardiol*. 2001;38:199-205.
- 13. Tsay SL, Chao YF. Effects of perceived self-efficacy and functional status on depression in patients with chronic heart failure. *J Nurs Res.* 2002;10:271-278.
- 14. Faris R, Purcell H, Henein MY, Coats AJ. Clinical depression is common and significantly associated with reduced survival in patients with non-ischaemic heart failure. *Eur J Heart Fail*. 2002;4:541-551.
- 15. Shabetai R. Depression and heart failure. *Psychosom Med.* 2002;64:13-14.
- 16. MacMahon KM, Lip GY. Psychological factors in heart failure: a review of the literature. *Arch Intern Med.* 2002;162:509-516.
- 17. Friedman MM, Griffin JA. Relationship of physical symptoms and physical functioning to depression in patients with heart failure. *Heart Lung*. 2001;30:98-104.
- **18.** Koenig HG. Depression in hospitalized older patients with congestive heart failure. *Gen Hosp Psychiatry*. 1998;20:29-43.

- 19. Murberg TA, Bru E, Aarsland T, Svebak S. Functional status and depression among men and women with congestive heart failure. *Int J Psychiatry Med*. 1998;28:273-291.
- **20.** Faris R, Purcell H, Henein MY, Coats AJ. Clinical depression is common and significantly associated with reduced survival in patients with non-ischaemic heart failure. *Eur J Heart Fail*. 2002;4:451-551.
- 21. Freedland KE, Rich MW, Skala JA, Carney RM, Davila-Roman VG, Jaffe AS. Prevalence of depression in hospitalized patients with congestive heart failure. *Psychosom Med.* 2003;65:119-128.
- Jiang W, Alexander J, Christopher E, Kuchibhatla M, Gaulden LH, Cuffe MS, Blazing MA, Davenport C, Califf RM, Krishnan RR, O'Connor CM. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. *Arch Intern Med.* 2001;161:1849-1856.
- 23. Skotzko CE, Krichten C, Zietowski G, Alves L, Freudenberger R, Robinson S, Fisher M, Gottlieb SS. Depression is common and precludes accurate assessment of functional status in elderly patients with congestive heart failure. *J Card Fail*. 2000;6:300-305.
- 24. Gottlieb SS, Khatta M, Friedmann E, Einbinder L, Katzen S, Baker B, Marshall J, Minshall S, Robinson S, Fisher ML, Potenza M, Sigler B, Baldwin C, Thomas SA. The influence of age, gender, and race on the prevalence of depression in heart failure patients. *J Am Coll Cardiol*. 2004;43:1542-1549.
- **25.** Freedland KE, Carney R, Rich MW. Depression in elderly patients with congestive heart failure. *J Geriatr Psychiatry*. 1991;24.
- 26. Barlow DH. Anxiety and its disorders. New York: Guilford Press; 1988.
- 27. Kubzansky LD, Kawachi I, Weiss ST, Sparrow D. Anxiety and coronary heart disease: a synthesis of epidemiological, psychological, and experimental evidence. *Ann Behav Med.* 1998;20:47-58.
- 28. Lewis MA, Haviland JM, eds. Fear and anxiety as emotional phenomena: Clinical phenomenology, evolutionary perspectives, and information-processing mechanisms. New York: Guilford Press; 1993. Handbook of Emotions.
- 29. Smith TW, Ruiz JM. Psychosocial influences on the development and course of coronary heart disease: current status and implications for research and practice. *J Consult Clin Psychol.* 2002;70:548-568.
- 30. De Jong MJ, Moser DK, An K, Chung ML. Anxiety is not manifested by elevated heart rate and blood pressure in acutely ill cardiac patients. *Eur J Cardiovasc Nurs*. in press.
- 31. Moser DK, Dracup K, Doering L, Evangelista L, Zambroski CH, Chung ML, Lennie TA, Westlake C, Heo S. Depression, anxiety, hostility and perceived control in elderly cardiac patients: Comparison of prevalence in heart failure, myocardial infarction, coronary artery bypass graft surgery, and healthy elders. in review.
- 32. Denollet J, Brutsaert DL. Personality, disease severity, and the risk of long-term cardiac events in patients with a decreased ejection fraction after myocardial infarction. *Circulation*. 1998;97:167-173.

- 33. Riedinger MS, Dracup KA, Brecht ML. Quality of life in women with heart failure, normative groups, and patients with other chronic conditions. *Am J Crit Care.* 2002;11:211-219.
- 34. Januzzi JL, Jr., Stern TA, Pasternak RC, DeSanctis RW. The influence of anxiety and depression on outcomes of patients with coronary artery disease. *Arch Intern Med.* 2000;160:1913-1921.
- **35.** Kubzansky LD, Kawachi I. Going to the heart of the matter: do negative emotions cause coronary heart disease? *J Psychosom Res.* 2000;48:323-337.
- 36. Kubzansky LD, Kawachi I, Spiro A, 3rd, Weiss ST, Vokonas PS, Sparrow D. Is worrying bad for your heart? A prospective study of worry and coronary heart disease in the Normative Aging Study. *Circulation*. 1997;95:818-824.
- 37. Malan SS. Psychosocial adjustment following MI: current views and nursing implications. *J Cardiovasc Nurs*. 1992;6:57-70.
- 38. Mayou RA, Gill D, Thompson DR, Day A, Hicks N, Volmink J, Neil A. Depression and anxiety as predictors of outcome after myocardial infarction. *Psychosom Med.* 2000;62:212-219.
- 39. Moser DK, Dracup K. Psychosocial recovery from a cardiac event: the influence of perceived control. *Heart Lung.* 1995;24:273-280.
- 40. Rozanski A, Bairey CN, Krantz DS, Friedman J, Resser KJ, Morell M, Hilton-Chalfen S, Hestrin L, Bietendorf J, Berman DS. Mental stress and the induction of silent myocardial ischemia in patients with coronary artery disease. *N Engl J Med*. 1988;318:1005-1012.
- 41. Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation*. 1999:99:2192-2217.
- 42. Rozanski A, Krantz DS, Bairey CN. Ventricular responses to mental stress testing in patients with coronary artery disease. Pathophysiological implications. *Circulation*. 1991;83:II137-144.
- 43. Moser DK, Worster PL. Effect of psychosocial factors on physiologic outcomes in patients with heart failure. *Journal of Cardiovascular Nursing*. 2000;14:106-115.
- 44. Clarke SP, Frasure-Smith N, Lesperance F, Bourassa MG. Psychosocial factors as predictors of functional status at 1 year in patients with left ventricular dysfunction. *Research in Nursing and Health*. 2000;23:290-300.
- 45. Konstam V, Salem D, Pouleur H, Kostis J, Gorkin L, Shumaker S, Mottard I, Woods P, Konstam MA, Yusuf S. Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. *American Journal of Cardiology*. 1996;78:890-895.
- **46.** Denollet J, Brutsaert DL. Personality, disease severity, and the risk of long-term cardiac events in patients with a decreased ejection fraction after myocardial infarction. *Circulation*. 1998;97:167-173.
- 47. Frasure-Smith N, Lesperance F, Talajic M. The impact of negative emotions on prognosis following myocardial infarction: is it more than depression? *Health Psychol.* 1995;14:388-398.

- 48. Herrmann C, Brand-Driehorst S, Kaminsky B, Leibing E, Staats H, Ruger U. Diagnostic groups and depressed mood as predictors of 22-month mortality in medical inpatients. *Psychosom Med.* 1998;60:570-577.
- 49. Moser DK, Dracup K. Is anxiety early after myocardial infarction associated with subsequent ischemic and arrhythmic events? *Psychosom Med.* 1996;58:395-401.
- 50. Lane D, Carroll D, Ring C, Beevers DG, Lip GY. Effects of depression and anxiety on mortality and quality-of-life 4 months after myocardial infarction. *J Psychosom Res.* 2000;49:229-238.
- 51. Lane D, Carroll D, Ring C, Beevers DG, Lip GY. Do depression and anxiety predict recurrent coronary events 12 months after myocardial infarction? *QJM*. 2000;93:739-744.
- **52.** Welin C, Lappas G, Wilhelmsen L. Independent importance of psychosocial factors for prognosis after myocardial infarction. *J Intern Med.* 2000;247:629-639.
- 53. Herrmann C, Brand-Driehorst S, Buss U, Ruger U. Effects of anxiety and depression on 5-year mortality in 5,057 patients referred for exercise testing. *J Psychosom Res.* 2000;48:455-462.
- **54.** Carney RM, Freedland KE, Stein PK. Anxiety, depression, and heart rate variability. *Psychosom Med.* 2000;62:84-87.
- 55. Lesperance F, Frasure-Smith N. Negative emotions and coronary heart disease: getting to the heart of the matter. *Lancet*. 1996;347:414-415.
- 56. Sheps DS, Sheffield D. Depression, anxiety, and the cardiovascular system: the cardiologist's perspective. *J Clin Psychiatry*. 2001;62 Suppl 8:12-16; discussion 17-18.
- 57. Sirois BC, Burg MM. Negative emotion and coronary heart disease. A review. *Behav Modif.* 2003;27:83-102.
- **58.** Daly PA, Sole MJ. Myocardial catecholamines and the pathophysiology of heart failure. *Circulation*. 1990;82:I35-43.
- 59. Medich C, Stuart EM, Deckro JP, Friedman R. Psychophysiologic control mechanisms in ischemic heart disease: the mind-heart connection. *J Cardiovasc Nurs.* 1991;5:10-26.
- 60. Veith RC, Lewis N, Linares OA, Barnes RF, Raskind MA, Villacres EC, Murburg MM, Ashleigh EA, Castillo S, Peskind ER, et al. Sympathetic nervous system activity in major depression. Basal and desipramine-induced alterations in plasma norepinephrine kinetics. *Arch Gen Psychiatry*. 1994;51:411-422.
- 61. Fehder WP. Alterations in immune response associated with anxiety in surgical patients. *CRNA*. 1999;10:124-129.
- 62. Carney RM, Blumenthal JA, Stein PK, Watkins L, Catellier D, Berkman LF, Czajkowski SM, O'Connor C, Stone PH, Freedland KE. Depression, heart rate variability, and acute myocardial infarction. *Circulation*. 2001;104:2024-2028.
- 63. Musselman DL, Evans DL, Nemeroff CB. The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. *Arch Gen Psychiatry*. 1998;55:580-592.
- 64. Ferguson DW, Berg WJ, Sanders JS. Clinical and hemodynamic correlates of sympathetic nerve activity in normal humans and patients with heart failure: evidence from direct microneurographic recordings. *J Am Coll Cardiol*. 1990;16:1125-1134.

- Stein PK, Carney RM, Freedland KE, Skala JA, Jaffe AS, Kleiger RE, Rottman JN. Severe depression is associated with markedly reduced heart rate variability in patients with stable coronary heart disease. *J Psychosom Res.* 2000;48:493-500.
- 66. Krittayaphong R, Cascio WE, Light KC, Sheffield D, Golden RN, Finkel JB, Glekas G, Koch GG, Sheps DS. Heart rate variability in patients with coronary artery disease: Differences in patients with higher and lower depression scores. *Psychosom Med.* 1997;59:231-235.
- 67. Kohn LM, Sleet DA, Carson JC, Gray RT. Life changes and urinary norepinephrine in myocardial infarction. *J Human Stress*. 1983;9:38-45.
- 68. Yeung AC, Vekshtein VI, Krantz DS, Vita JA, Ryan TJ, Jr., Ganz P, Selwyn AP. The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. *N Engl J Med.* 1991;325:1551-1556.
- 69. Watkins LL, Blumenthal JA, Carney RM. Association of anxiety with reduced baroreflex cardiac control in patients after acute myocardial infarction. *Am Heart J.* 2002;143:460-466.
- 70. Hjemdahl P, Larsson PT, Wallen NH. Effects of stress and beta-blockade on platelet function. *Circulation*. 1991;84:VI-44-VI-61.
- 71. Markovitz JH, Matthews KA. Platelets and coronary heart disease: potential psychophysiologic mechanisms. *Psychosom Med.* 1991;53:643-668.
- 72. Patterson SM, Krantz DS, Gottdiener JS, Hecht G, Vargot S, Goldstein DS. Prothrombotic effects of environmental stress: changes in platelet function, hematocrit, and total plasma protein. *Psychosom Med.* 1995;57:592-599.
- 73. Jern C, Eriksson E, Tengborn L, Risberg B, Wadenvik H, Jern S. Changes of plasma coagulation and fibrinolysis in response to mental stress. *Thrombosis & Haemostasis*. 1989;62:767-771.
- 74. Grignani G, Soffiantino F, Zucchella M, Pacchiarini L, Tacconi F, Bonomi E, Pastoris A, Sbaffi A, Fratino P, Tavazzi L. Platelet activation by emotional stress in patients with coronary artery disease. *Circulation*. 1991;83:II-128-II-136.
- 75. Wallen NH, Held C, Rehnqvist N, Hjemdahl P. Effects of mental and physical stress on platelet function in patients with stable angina pectoris and healthy controls. *Eur Heart J.* 1997;18:807-815.
- von Kanel R, Mills PJ, Fainman C, Dimsdale JE. Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: a biobehavioral pathway to coronary artery disease? *Psychosom Med.* 2001;63:531-544.
- 77. Middlekauff HR, Mark AL. The treatment of heart failure: the role of neurohumoral activation. *Intern Med.* 1998;37:112-122.
- 78. Lown B, Verrier RL. Neural activity and ventricular fibrillation. *N Engl J Med*. 1976;294:1165-1170.
- 79. Lown B, Verrier RL, Rabinowitz SH. Neural and psychologic mechanisms and the problem of sudden cardiac death. *Am J Cardiol.* 1977;39:890-902.
- 80. Tavazzi L, Zotti AM, Rondanelli R. The role of psychologic stress in the genesis of lethal arrhythmias in patients with coronary artery disease. *Eur Heart J.* 1986;7 Suppl A:99-106.
- 81. Lown B. Sudden cardiac death: biobehavioral perspective. *Circulation*. 1987;76:I-186-I-196.

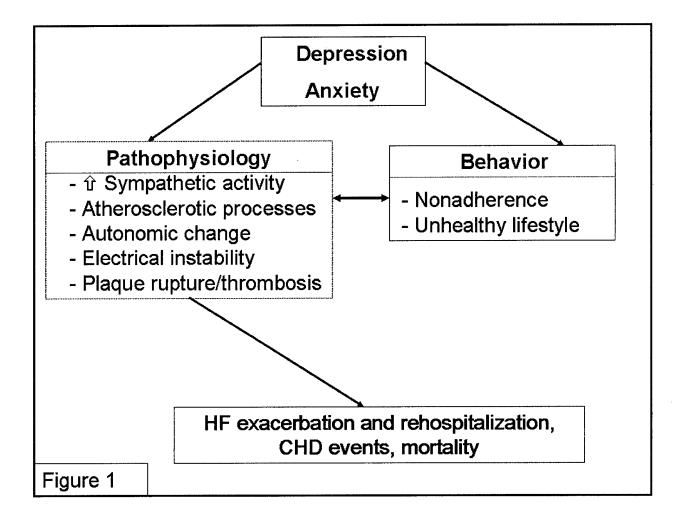
- 82. Brodsky MA, Sato DA, Iseri LT, Wolff LJ, Allen BJ. Ventricular tachyarrhythmia associated with psychological stress: the role of the sympathetic nervous system. *JAMA*. 1987;257:2064-2067.
- 83. Krantz DS, Kop WJ, Santiago HT, Gottdiener JS. Mental stress as a trigger of myocardial ischemia and infarction. *Cardiol Clin.* 1996;14:271-287.
- 84. Mittleman MA, Maclure M, Sherwood JB, Mulry RP, Tofler GH, Jacobs SC, Friedman R, Benson H, Muller JE. Triggering of acute myocardial infarction onset by episodes of anger. *Circulation*. 1995;92:1720-1725.
- 85. Kop WJ. Chronic and acute psychological risk factors for clinical manifestations of coronary artery disease. *Psychosom Med.* 1999;61:476-487.
- 86. Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation*. 1999;99:2192-2217.
- 87. L'Abbate A, Simonetti I, Carpeggiani C, Michelassi C. Coronary dynamics and mental arithmetic stress in humans. *Circulation*. 1991;83:II-94-II-99.
- 88. Papademetriou V, Gottdiener JS, Kop WJ, Howell RH, Krantz DS. Transient coronary occlusion with mental stress. *Am Heart J.* 1996;132:1299-1301.
- **89.** Gelernt MD, Hochman JS. Acute myocardial infarction triggered by emotional stress. *Am J Cardiol*. 1992;69:1512-1513.
- 90. Vita JA, Treasure CB, Yeung AC, Vekshtein VI, Fantasia GM, Fish RD, Ganz P, Selwyn AP. Patients with evidence of coronary endothelial dysfunction as assessed by acetylcholine infusion demonstrate marked increase in sensitivity to constrictor effects of catecholamines. *Circulation*. 1992;85:1390-1397.
- 91. Legault SE, Freeman MR, Langer A, Armstrong PW. Pathophysiology and time course of silent myocardial ischaemia during mental stress: clinical, anatomical, and physiological correlates. *Br Heart J.* 1995;73:242-249.
- 92. Kop WJ, Krantz DS, Howell RH, Ferguson MA, Papademetriou V, Lu D, Popma JJ, Quigley JF, Vernalis M, Gottdiener JS. Effects of mental stress on coronary epicardial vasomotion and flow velocity in coronary artery disease: relationship with hemodynamic stress responses. *J Am Coll Cardiol*. 2001;37:1359-1366.
- 93. Gottdiener JS, Krantz DS, Howell RH, Hecht GM, Klein J, Falconer JJ, Rozanski A. Induction of silent myocardial ischemia with mental stress testing: relation to the triggers of ischemia during daily life activities and to ischemic functional severity. *J Am Coll Cardiol*. 1994;24:1645-1651.
- 94. Mazzuero G, Temporelli PL, Tavazzi L. Influence of mental stress on ventricular pump function in postinfarction patients. An invasive hemodynamic investigation. *Circulation*. 1991;83:II145-154.
- 95. Goldberg AD, Becker LC, Bonsall R, Cohen JD, Ketterer MW, Kaufman PG, Krantz DS, Light KC, McMahon RP, Noreuil T, Pepine CJ, Raczynski J, Stone PH, Strother D, Taylor H, Sheps DS. Ischemic, hemodynamic, and neurohormonal responses to mental and exercise stress: experience from the Psychophysiological Investigations of Myocardial Ischemia Study (PIMI). *Circulation*. 1996;94:2402-2409.
- 96. Jain D, Shaker SM, Burg M, Wackers FJ, Soufer R, Zaret BL. Effects of mental stress on left ventricular and peripheral vascular performance in patients with coronary artery disease. *J Am Coll Cardiol*. 1998;31:1314-1322.

- 97. Kuroda T, Kuwabara Y, Watanabe S, Nakaya J, Hasegawa R, Shikama T, Matsuno K, Mikami Y, Fujii K, Saito T, Masuda Y. Effect of mental stress on left ventricular ejection fraction and its relationship to the severity of coronary artery disease. *Eur J Nucl Med.* 2000;27:1760-1767.
- 98. Vinson JM, Rich MW, Sperry JC, Shah AS, McNamara T. Early readmission of elderly patients with congestive heart failure. *J Am Geriatr Soc.* 1990;38:1290-1295.
- 99. Bennett SJ, Huster GA, Baker SL, Milgrom LB, Kirchgassner A, Birt J, Pressler ML. Characterization of the precipitants of hospitalization for heart failure decompensation. *Am J Crit Care*. 1998;7:168-174.
- 100. Chin MH, Goldman L. Correlates of early hospital readmission or death in patients with congestive heart failure. *Am J Cardiol*. 1997;79:1640-1644.
- 101. Ghali JK, Kadakia S, Cooper R, Ferlinz J. Precipitating factors leading to decompensation of heart failure. Traits among urban blacks. *Arch Intern Med.* 1988;148:2013-2016.
- 102. Michalsen A, Konig G, Thimme W. Preventable causative factors leading to hospital admission with decompensated heart failure. *Heart*. 1998;80:437-441.
- 103. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Avorn J. Noncompliance with congestive heart failure therapy in the elderly. *Arch Intern Med.* 1994;154:433-437.
- 104. Horwitz RI, Viscoli CM, Berkman L, Donaldson RM, Horwitz SM, Murray CJ, Ransohoff DF, Sindelar J. Treatment adherence and risk of death after a myocardial infarction. *Lancet*. 1990;336:542-545.
- 105. Gallagher EJ, Viscoli CM, Horwitz RI. The relationship of treatment adherence to the risk of death after myocardial infarction in women. *JAMA*. 1993;270:742-744.
- 106. Dew MA, Kormos RL, Roth LH, Murali S, DiMartini A, Griffith BP. Early post-transplant medical compliance and mental health predict physical morbidity and mortality one to three years after heart transplantation. *J Heart Lung Transplant*. 1999;18:549-562.
- 107. McDermott MM, Schmitt B, Wallner E. Impact of medication nonadherence on coronary heart disease outcomes. A critical review. *Arch Intern Med.* 1997;157:1921-1929.
- **108.** Ghali JK. Heart failure and noncompliance in the elderly. *Arch Intern Med.* 1994;154:2109-2110.
- 109. Carney RM, Freedland KE, Eisen SA, Rich MW, Jaffe AS. Major depression and medication adherence in elderly patients with coronary artery disease. *Health Psychol.* 1995;14:88-90.
- 110. Ziegelstein RC, Fauerbach JA, Stevens SS, Romanelli J, Richter DP, Bush DE. Patients with depression are less likely to follow recommendations to reduce cardiac risk during recovery from a myocardial infarction. *Arch Intern Med*. 2000;160:1818-1823.
- 111. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med.* 2000;160:2101-2107.
- 112. Jacob S, Sebastian JC, Abraham G. Depression and congestive heart failure: are antidepressants underutilized? *Eur J Heart Fail*. 2003;5:399-400.

- 113. Banazak DA. Minor depression in primary care. J Am Osteopath Assoc. 2000;100:783-787.
- 114. Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT, Jr., Krishnan KR, van Zyl LT, Swenson JR, Finkel MS, Landau C, Shapiro PA, Pepine CJ, Mardekian J, Harrison WM, Barton D, McLvor M. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA*. 2002;288:701-709.
- 115. Roose SP. Considerations for the use of antidepressants in patients with cardiovascular disease. *Am Heart J.* 2000;140:84-88.
- 116. Roose SP. Depression, anxiety, and the cardiovascular system: the psychiatrist's perspective. *J Clin Psychiatry*. 2001;62 Suppl 8:19-22; discussion 23.
- 117. Roose SP. Treatment of depression in patients with heart disease. *Biol Psychiatry*. 2003;54:262-268.
- 118. Murberg TA, Bru E. Social relationships and mortality in patients with congestive heart failure. *J Psychosom Res.* 2001;51:521-527.
- 119. Konstam V, Salem D, Pouleur H, Kostis J, Gorkin L, Shumaker S, Mottard I, Woods P, Konstam MA, Yusuf S. Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. SOLVD Investigations. Studies of Left Ventricular Dysfunction Investigators. *Am J Cardiol.* 1996;78:890-895.
- 120. Reker GT. Personal meaning, optimism and choice: Existential predictors of depression in community and institutional elderly. *The Gerontologist.* 1997;37.
- 121. Lantz J, Gomia L. Activities and stages in existential psychotherapy with older adults. *Clin Gerontol*. 1995;16:31-40.
- 122. Konstam V, Holmes W, Wilczenski F, Baliga S, Lester J, Priest R. Meaning in the lives of caregivers of individuals with Parkinson's Disease. *J Clin Psychol Med Settings*. 2003;10.
- 123. Dracup K, Westlake C, Erickson VS, Moser DK, Caldwell ML, Hamilton MA. Perceived control reduces emotional stress in patients with heart failure. *J Heart Lung Transplant*. 2003;22:90-93.
- 124. Oxman TE, Hull JG. Social support, depression, and activities of daily living in older heart surgery patients. *J Gerontol B Psychol Sci Soc Sci.* 1997;52:P1-14.
- 125. Ruiz BA, Dibble SL, Gilliss CL, Gortner SR. Predictors of general activity 8 weeks after cardiac surgery. *Appl Nurs Res.* 1992;5:59-65.
- 126. Perkins S, Jenkins LS. Self-efficacy expectation, behavior performance, and mood status in early recovery from percutaneous transluminal coronary angioplasty. *Heart Lung.* 1998;27:37-46.
- 127. Thompson SC, Sobolew-Shubin A, Galbraith ME, Schwankovsky L, Cruzen D. Maintaining perceptions of control: finding perceived control in low-control circumstances. *J Pers Soc Psychol.* 1993;64:293-304.
- 128. Thompson SC. Will it hurt less if i can control it? A complex answer to a simple question. *Psychol Bull.* 1981;90:89-101.
- 129. Bohachick P, Taylor MV, Sereika S, Reeder S, Anton BB. Social support, personal control, and psychosocial recovery following heart transplantation. *Clin Nurs Res.* 2002;11:34-51.

- **130.** Taylor SE, Helgeson VS, Reed GM, Skokan LA. Self-generated feelings of control and adjustment to physical illness. *J Soc Issues*. 1991;47:91-109.
- 131. Ben-Sira Z, Eliezer R. The structure of readjustment after heart attack. *Soc Sci Med.* 1990;30:523-536.
- 132. Erhardt L, Cline C. Heart failure clinics: a possible means of improving care. *Heart*. 1998;80:428-429.
- 133. Murberg TA, Bru E, Aarsland T, Svebak S. Social support, social disability and their role as predictors of depression among patients with congestive heart failure. *Scand J Soc Med.* 1998;26:87-95.
- 134. Krumholz HM, Butler J, Miller J, Vaccarino V, Williams CS, Mendes de Leon CF, Seeman TE, Kasl SV, Berkman LF. Prognostic importance of emotional support for elderly patients hospitalized with heart failure. *Circulation*. 1998;97:958-964.
- 135. Nieboer AP, Schulz R, Matthews KA, Scheier MF, Ormel J, Lindenberg SM. Spousal caregivers' activity restriction and depression: a model for changes over time. *Soc Sci Med.* 1998;47:1361-1371.
- 136. Lyons RF, Sullivan MJL, Ritvo PG, Coyne JC. Relationships in chronic illness and disability. Thousand Oaks: Sage; 1995.
- 137. Coyne JC, Smith DA. Couples coping with a myocardial infarction: a contextual perspective on wives' distress. *J Pers Soc Psychol.* 1991;61:404-412.
- 138. Callahan HE. Families dealing with advanced heart failure: a challenge and an opportunity. *Crit Care Nurs Q.* 2003;26:230-243.
- 139. Tix AP, Frazier PA. The use of religious coping during stressful life events: Main effects, moderation, and mediation. *J Consult Clin Psychol*. 1998;66.
- 140. Powell LH, Shahabi L, Thoreson CE. Religion and spirituality: Linkages to physical health. *Am Psychol*. 2003;58:36-52.
- 141. Freedland KE. Religious beliefs shorten hospital stays? Psychology works in mysterious ways: comment on Contrada et al. (2004). *Health Psychol*. 2004;23:239-242.
- **142.** Sherman AC, Simonton S. Coping with cancer in the family. *J Counsel Therapy Couples Families*. 2001;9.
- 143. Contrada RJ, Idler EL, Goyal TM, Cather C, Rafalson L, Krause TJ. Why not find out whether religious beliefs predict surgical outcomes? If they do, why not find out why? Reply to Freedland (2004). *Health Psychol*. 2004;23:243-246.
- 144. Guck TP, Elsasser GN, Kavan MG, Barone EJ. Depression and congestive heart failure. *Congest Heart Fail.* 2003;9:163-169.

Figure 1: Potential mechanisms linking depression and anxiety with adverse cardiac outcomes



Legend: CHD = coronary heart disease events